



Antibiotic resistance in aquatic environments: implications for public health and aquaculture

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Received: 24 March 2025; Revised: 20 April 2025; Accepted: 27 April 2025; Published: 20 May 2025

Abstract

The emergence of Antibiotic Resistance (AR) and polyresistance in infectious agents poses a significant global health threat. AR bacteria pose a potential Public Health (PH) threat due to their immediate spread to people by ingesting infected food or water or spreading their AR genomes to harmful microbes linked to Aquatic Environments (AE). Aquaculture is vital to address contemporary issues, including the demand for protein to sustain human populations and the imperative of environmental stewardship. The application of antibiotics in AE induces AR in the adjacent bacteria within the aquatic section, debris, and fish-associated bacteria cultures. Bacteria may disseminate AR genes and portable resistance genomes by crossing genes horizontally propagating genomic markers. Upon activation, AR rapidly disseminates throughout marine microbial populations and may infect public infectious bacteria, rendering antibiotic usage ineffective for PH. Strategies must be implemented to mitigate adverse effects on PH, with a decrease in the utilization of antibiotics as a central focus. The One Healthcare (OH) strategy, integrating diverse expertise in veterinary science, ecosystems, and healthcare while adhering to principles of sustainable development, is essential and highly advocated to address significant PH and ecological safety concerns in the AE.

Keywords: Antibiotic resistance, Aquatic environments, Bacteria, Genome, Public health, Aquaculture.

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DOI: 10.70102/IJARES/V5I1/5-1-62

Introduction

Antibiotics refer to a diverse array of chemical compounds generated by organic, partially synthetic, and artificial methods and are used to either suppress (bacteriostatic) or eradicate (bactericidal) bacterial development. They are classified according to their actions into two categories: bacterial-static or bactericides and by their range of effectiveness, as restricted or wide-ranging antibiotics (Larsson and Flach, 2022). The development of AR differs among regions and nations, correlating with the level of antibiotic usage, which is influenced and controlled by the antimicrobial regulations of each nation. China has been recognized as the foremost supplier and user of veterinary and human antibiotics globally (Mehrani *et al.*, 2016).

The antibiotic-related trouble is attributed to the improper use of antibacterial agents, which eventually get released into the AE, the existence of leftover antibiotics (either the parent compound or its derivatives) in animal byproducts and debris, and the insufficient regulation and oversight of antibiotic generation, usage, and elimination. Human behaviors related to economic development significantly increased the prevalence of leftover antibiotics in food products and surroundings, as well as the emergence and dissemination of AR bacteria and their resistance genetics, resulting in a rise in the number of impermeable microbes and their genes (Lin *et al.*, 2021).

Antibiotic leftovers, AR bacteria, and resistance genomes are considered ecological contaminants and are

responsible for a persistent PH concern worldwide (Li and Zhang, 2022). The health issues associated with AR microbes mostly stem from limited therapeutic options in many underdeveloped nations that do not have a source of high-quality treatment, hence highlighting infection as a significant cause of morbidity and death (Biswas *et al.*, 2021). The soil and AE are considered crucial repositories and causes of AR, particularly due to the influence of aquaculture. The application of antibacterial agents in livestock that produce food not only promotes AR but may also lead to antibiotic leftovers involving parent molecules or their derivatives in animal-based goods such as muscle, kidney, and eggs intended for consumption by people (Dülger and Dülger, 2022).

Nonetheless, leftover antibiotics have been shown to significantly adversely affect PH concerning toxicology, immunopathological disorders, cancer-causing potential, allergic responses, and drug sensitivity, among other issues (Grenni, 2022). The detrimental effects are often shaped by land utilization, polluted water supplies, national policies related to manufacturing, commerce, livestock welfare, food safety, international business, animal demographics, and human relationships, which reportedly differ significantly across areas and nations (Rahman *et al.*, 2021).

AR is recognized as an "OH issue," serving as an explanation and a remedy involving connections among individuals, animals, and the surroundings (Jiang *et al.*, 2022). In response to AR, the World Health

Organization (WHO) established a Global Action Strategy (GAS) requiring every country to formulate national action plans aligned with the GAS's primary goals and tailored to their financial capabilities and specific challenges (Chaturvedi *et al.*, 2021; Zhu *et al.*, 2024). Tracking and surveillance of antibiotic usage and resistance constitute one aspect of the plans to combat AR (Ramachandran, 2023). Nonetheless, developing and underdeveloped nations have difficulties monitoring systems due to insufficient capacity and connectivity.

Use of Antibiotics in Aquaculture

Antibiotics impede bacterial proliferation or eradicate cells of bacteria, constituting vital medications for PH since its inception (Adenaya *et al.*, 2023). The European Medicinal Agency defines antibiotics as "any medication having a direct effect on microorganisms utilized for therapy or mitigation of illnesses or infectious diseases." Antibiotics are complex compounds, including many different functions in their structures, and are categorized into distinct classes based on their modes of operation.

Antibiotics combat bacteria in several ways, including inhibiting cell wall production, altering the exterior of cells, inhibiting the formation of proteins, inhibiting amino acid synthesizing, aggressive antagonism, and exhibiting antimetabolite action (Pepi and Focardi, 2021). Besides their application in human medical care, antibiotics are extensively utilized in livestock medicine to enhance animal health, particularly in aquaculture, a prominent industry.

Antibiotics are utilized in aquaculture for various objectives: (i) Preventive: The provision of drugs to all animals in a

group to avert diseases before their onset, utilizing antibiotics at sub-therapeutic access levels; (ii) Therapy: The provision of drugs to address the ailments of ill livestock; (iii) Metaphylactic: The application of mass medicine to eradicate or mitigate a predicted illness breakout; (iv) Development boosters: Given to animals to enhance growth rates and nutrition conversion effectiveness.

Development of AR

Antibiotic leftovers may favor the emergence of AR bacteria in AE, facilitating the proliferation of AR, regardless of doses within the minimal inhibitory level of the group's strains of bacteria (Vij and Prashant, 2024). Elevated levels of AR bacteria have been documented in locations adjacent to aquaculture operations utilizing antibiotics, indicating that altering antibiotics in aquaculture facilities significantly contributes to selective strains and enhances the prevalence of AR among surrounding bacterial communities. Ninety percent of AE bacteria exhibit resistance to not less than one antibiotic, while roughly twenty percent are resistant to several antibiotics.

The concurrent use of many antibiotics in aquaculture may lead to the emergence of multidrug-resistant microorganisms. Bacteria with genes that encode for new AR pathways were also found. AR enables microorganisms to endure elevated levels of antibiotics, providing a selection advantage to individuals within populations with such resistances. Resistant isolates of bacteria dominate vulnerable strains. A significant and concerning element is that the antibiotics employed in aquaculture are also utilized in PH, hence fostering

resistance to these medicines. In coastal aquaculture operations, the improper use of antibiotics has led to elevated concentrations of these substances in the adjacent sands and water section. The application of antibiotics in coastal European seabeds (D. labrax) includes oxytetracycline and promoted sulfur amides, demonstrating metaphylaxis as the optimal behavior for their administration following the identification of infection and clinical illness in a subset of the group.

Dissemination of AR Among Bacteria

Aquaculture areas serve as 'areas for AR genomes.' Depending on environmental conditions, bacteria with various AR genomes may proliferate, disseminating genes across diverse locations. The AE may include infectious bacteria from humans and animals, which facilitate the exchange of biological characteristics between AE and terrestrial microorganisms. The collection of transmissible genetic components inside a genome is called a mobilome and may disseminate across AE bacteria.

Lateral mutations between AE and human infectious agents are a significant occurrence involving AR genomes. Consequently, novel genetic components may infiltrate soil bacterial populations, including human diseases, making them more challenging to treat. AE with aquaculture operations may provide distinct circumstances that facilitate gene crossing horizontally. A case involves biological films of AE bacteria adhering to biological particulates, debris, sands, and AE alongside substantial levels of microorganisms and mutational agents in

ocean water, facilitating horizontal gene exchange and the propagation of AR.

In AE, the horizontal exchange of genes may be facilitated by DNA released during bacterial breakdown and by polymers. Freestanding DNA from microbes and vectors may carry AR genes that can be activated upon entering bacterial cells. AE bacteria, like *Vibrio* spp., have intrinsic DNA absorption competence, facilitating AE conversion. AR genes have varying durability in the natural world, contingent upon their vector or genomic background. AR genomes derived from plasmids have greater mobility and quantities than those originating from genomes.

AR genes exist in both internal and external DNA components within the surroundings. Internal and external AR genomes exhibit the same pathways in debris at an AE facility and adjacent locations, indicating the existence of links between these diverse sites. The properties of DNA strands also influence the longevity of AR genomes in the external milieu. Certain external AR genomes exhibit greater resistance to DNA disintegrating agents than others, presumably owing to their sequencing and physical features. Chromosomal DNA exhibits more absorptivity than viral DNA due to its elevated charges on its surface and increased molecular versatility. Consequently, external genomes may last in the surroundings for a longer duration than external viral DNA. A reduced discovery rate for external DNA associated with plasmids is anticipated in debris compared to chromosomal DNA.

Combination

Internal AR genomes may be transmitted by recombination via contact between cells and translation due to bacterial phage contamination. The combination is a transfer of genes horizontally, a process that occurs via direct contact among cells via junctions formed by pili, employing a pore. The combination is linked to vectors that may transmit more rapidly than the entire chromosome. More than half of the identified vectors may be transmitted by crosslinking as a means of horizontal transmission of genes.

The combination can happen within the identical type of bacteria or across separate species with significant phylogenetic distance but at a lower frequency. Vectors and transposons enable the conjugative transmission of AR by acquiring AR genomes and transporting them to the intended cells. The combination of AR genomes has often been documented across several settings, such as the soil, debris, water, food, plants, animals, and clinical microorganisms—the conjugative transmission of multiple medications across and amongst microorganisms in various settings, as depicted in Figure 1A.

Translation

Translation is a horizontal gene crossover method whereby microbes facilitate the transfer of internal DNA from a contaminated bacteria cell to a target bacterial cell. Bacteriophages are viruses that attack bacteria and may acquire and transmit genes to a host bacterium. These microbes are capable of transferring both genomic and vector DNA. Following DNA exchange, it must be integrated into its destination

genome by identical recombination. Certain bacteria have a broad spectrum of microbial carriers and may traverse many species. In the initial stage, bacterial phages adhere to the microbial host and subsequently implant their genetic code, which may commandeer the host's molecular structure to produce more vectors. Subsequent vectors may destroy the host cell and disseminate into the surroundings, as given in Figure 1B.

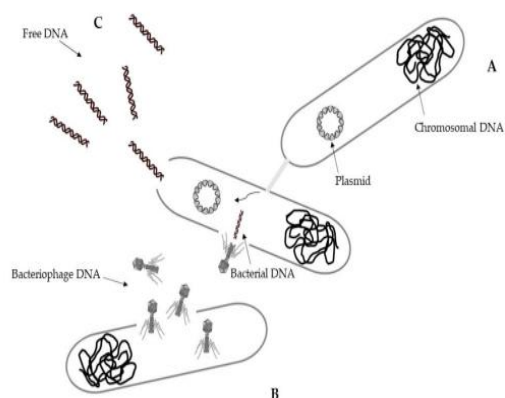


Figure 1: Horizontal gene crossover method
(A) Combination (B) Translation (C) Metamorphosis.

Metamorphosis

Unlike internal DNA, external AR genes may infiltrate the appropriate cells of non-resistant organisms via organic transition. Extracellular genomes may arise from the dissolution of deceased cells and the release from viable cells, constituting an active gene reservoir for organic metamorphosis. Adsorption onto debris particles, sand grains, mineral clay, and humus may safeguard external DNA against enzymatic nuclease degradation.

Natural change denotes the direct acquisition and incorporation of external DNA. Cells from bacteria must first develop a controlled biological state, a specific ability condition, to perform spontaneous changes. Particular factors

in the environment may foster the formation of abilities. External DNA acquisition by capable cells may be attributed to nutritional needs, genome repair, and genetic diversity for evolutionary purposes. Natural change necessitates DNA stability in the external milieu and its capacity to withstand breakdown under environmental circumstances.

The enhanced effectiveness of biological transition is seen when extended external DNA fragments are present, compared to the outcomes observed with shorter external DNA segments. Upon entering the receiving cell, the fresh DNA must be incorporated into the target microbial genome if it is chromatin DNA or embedded or recircularized into a self-reproducing vector if it is vector DNA. Natural translation via chromosomal DNA is thus more effective than vector DNA, as depicted in Figure 1C.

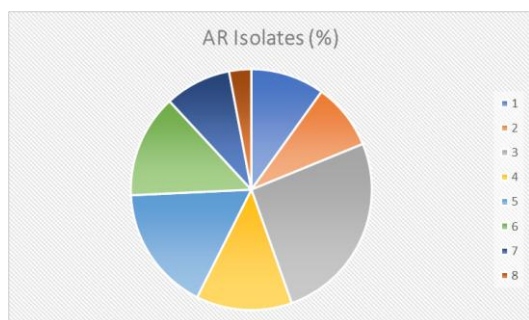


Figure 2: Multiple AR in *Vibrio* isolates (%) collected from sources in AE.

Figure 2 elucidates the distribution of multidrug AR among *Vibrio* isolates obtained from AE. Significantly, the largest proportion (26%) of isolates exhibited resistance to three classes of antibiotics, suggesting a considerable prevalence of intermediate multidrug resistance in these aquatic habitats. This tendency indicates that exposure to three distinct classes of antibiotics may be

prevalent in these ponds, perhaps resulting from frequent or unregulated antibiotic application in aquaculture. A significant proportion of isolates exhibited resistance to five (17%) and six (14%) classes of antibiotics, further highlighting the adaptive ability of *Vibrio* species to endure various antibiotic assaults.

Notably, resistance to either one or two classes of antibiotics was detected at comparatively low percentages (10% and 9%, respectively), indicating that isolates with modest resistance may be less common or less viable in antibiotic-saturated settings. Conversely, 3% of the isolates demonstrated resistance to all eight tested antibiotic classes, indicating the existence of highly resistant bacteria that significantly threaten PH and possibly population health via the food chain. The statistics underscore the need for monitoring and controlling antibiotic use in aquaculture to avert the proliferation of multidrug-resistant bacteria in AE.

Concluding Remarks

This study's results and discussions underscore the pressing need for a globally coordinated and interdisciplinary strategy to address the escalating issue of antibiotic resistance (AR) in aquatic environments (AE), especially within aquaculture. The use of antibiotics in aquaculture, while advantageous for disease control and production, has significantly facilitated the creation and spread of AR bacteria and genes in marine environments. The unregulated spread of AR bacteria presents significant PH problems since these bacteria may be transmitted via the food chain or environmental exposure,

reducing the efficacy of vital antibiotic treatments and increasing the danger of untreatable diseases.

The work highlights the intricate mechanisms—specifically the horizontal transmission of gene methods, including combination, metamorphosis, and transduction—by which resistance characteristics disseminate throughout microbial populations in aquatic environments. The enduring presence of AR genes in sediments, AE, and fish-associated biofilms further exemplifies the ecological durability of these hazards. The existence of *Vibrio* isolates resistant to several antibiotic classes, including those used in human medicine, underscores the vital connection between environmental microbiology and public health. To address this growing problem, it is essential to implement the One Health (OH) plan, fostering intersectoral cooperation among environmental research, veterinary medicine, and human health. To mitigate AR threats, preserve marine biodiversity, and protect future generations from the repercussions of a post-antibiotic era, it is imperative to develop sustainable aquaculture policies, enforce severe antibiotic laws, improve waste management, and increase monitoring systems collectively.

Alongside legislative and monitoring efforts, emerging technical options, including nanotechnology-based antimicrobials, probiotics, vaccinations, and CRISPR-based gene editing, provide viable alternatives to conventional antibiotics in aquaculture. These methods may markedly diminish the selection pressure that promotes resistance development while preserving fish health and production efficiency. Moreover,

using artificial intelligence (AI) and machine learning algorithms for early disease detection and optimization of antibiotic use may result in more data-driven and accurate aquaculture management. New technology may facilitate the shift towards precision aquaculture, reducing environmental impact while guaranteeing food security and economic sustainability.

Public education and stakeholder involvement are essential elements of a sustainable approach to mitigating AR. Equipping aquaculture producers with training on ethical antibiotic use, biosecurity measures, and alternative therapies cultivates a culture of responsibility and awareness. Consumers significantly influence demand for sustainably produced, antibiotic-free seafood via educated choices. Ultimately, tackling AR in AE is not only a scientific or regulatory issue but a social one necessitating collaboration across all tiers—from local farmers to global governing entities. This work offers a basic viewpoint for further multidisciplinary research and collaborative efforts to ensure the long-term health of aquatic ecosystems and PH.

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